

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Jeannette Whitcomb

Serial No.: 09/320,299

Examiner: Not Yet Known

Filed : May 26, 1999

Group Art Unit: 1643

For :

MEANS AND METHODS FOR MONITORING NON-NUCLEOSIDE  
REVERSE TRANSCRIPTASE INHIBITOR ANTIRETROVIRAL  
THERAPY AND GUIDING THERAPEUTIC DECISION IN THE  
TREATMENT OF HIV/AIDS



1185 Avenue of the Americas  
New York, New York 10036  
December 22, 1999

Assistant Commissioner for Patents  
Washington, D.C. 20231

SIR:

INFORMATION DISCLOSURE STATEMENT

In accordance with her duty of disclosure under 37 C.F.R. §1.56, applicant would like to direct the Examiner's attention to the following documents which are listed below and on the accompanying PTO Form 1449 attached hereto as **Exhibit A**. Copies of these documents are attached hereto as **Exhibits 1-7**. Copies of documents numbered below **8-27** were previously cited or disclosed by applicants in co-assigned, co-pending U.S. Serial No. 09/085,148, filed May 26, 1998 in an Information Disclosure Statement filed January 8, 1999.

1. Sakar, G. and Sommer, S.S. (1990) "The "Megaprimer" Method of Site-Directed Mutagenesis" Biotechniques, **8(4):404-407** (Exhibit 1);

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2. Balzarini J, (1998) "A Novel Mutation (F227L) Arises in the Reverse Transcriptase of Human Immunodeficiency Virus Type 1 on Dose-Escalating Treatment of HIV Type 1-Infected Cell Cultures With the Nucleoside Reverse Transcriptase Inhibitor Thiocarboxanilide UC-781" AIDS, **14(3)**:255-260 (Exhibit 2);
3. Balzarini J, et al. (1997) "Zidovudine-Resistant Human Immunodeficiency Virus Type 1 Strains Subcultured in the Presence of Both Lamivudine and Quinoxaline HBV 097 Retain Marked Sensitivity to HBV 097 but not to Lamivudine" J of Infect Dis, **176**:1392-1397 (Exhibit 3);
4. De Clercq E, (1997) "Development of Resistance of Human Immunodeficiency Virus (HIV) to Anti-HIV Agents: How to Prevent the Problem" International J. of Antimicro Agnts, **9**:21-36 (Exhibit 4);
5. Pelemans H, et al. (1997) "Characteristics of the Pro225His Mutation in Human Immunodeficiency Virus Type 1 (HIV-1) Reverse Transcriptase That Appears Under Selective Pressure of Dose-Escalating Quinoxaline Treatment of HIV-1" J. Viro, **71(11)**:8195-8203 (Exhibit 5);
6. Shi C and Mellors JW, (1997) "A Recombinant Retroviral System For Rapid *In Vivo* Analysis of Human Immunodeficiency Virus Type I Susceptibility to Reverse Transcriptase Inhibitors" Antimicro Agnts and Chemotherp, **41(12)**:2781-2785 (Exhibit 6);
7. Strair RK, et al. (1993) "Recombinant Retroviral Systems For the Analysis of Drug Resistant HIV" Nucl Acids Res, **21(20)**: 4836-4842 (Exhibit 7);

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8. U.S. Patent No. 5,650,268, Kozal, Michael, J., and Merigan, Thomas, C. May 20, 1997;
9. U.S. Patent No. 5,631,128, Kozal, Michael, J., and Merigan, Thomas, C. (1997) May 20, 1997;
10. Arnold E., et al. (1995) "Structures of DNA and RNA Polymerases and Their Interactions with Nucleic Acid Substrates", Curr Opin Struct Biol 5:27-38;
11. Balzarini J., et al., (1992) "HIV-1-Specific Reverse Transcriptase Inhibitors Show Differential Activity Against HIV-1 Mutant Strains Containing Different Amino Acid Substitutions in the Reverse Transcriptase", Virology 192:246-253;
12. Cheeseman S.H., et al. (1995) "Phase I/II Evaluation of Nevirapine Alone and in Combination with Zidovudine for Infection with Human Immunodeficiency Virus", J Acquir Immune Defic Syndr 8:141-151;
13. D'Aquila R.T. (1994) "Molecular Pathogenesis and Laboratory Monitoring", Clin Lab Med 14:393-423;
14. DeJong, M.D., et al. (1994) "Alternating Nevirapine and Zidovudine Treatment of Human Immunodeficiency Virus Type 1-Infected Persons Does Not Prolong Nevirapine Activity", J Infect Dis 169:1346-1350;
15. Dueweke, T.J., et al. (1993) "A Mutation in Reverse Transcriptase of Bis (Heteroaryl) Piperazine Resistant Human Immunodeficiency Virus Type 1 That Confers Increased Sensitivity to Other Nonnucleoside Inhibitors", PNAS 90:4713-4717;

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16. Eastman, P. Scott, et al. (1995) "Monisotopic Hybridization Assay for Determination of Relative Amounts of Genotypic Human Immunodeficiency Virus Type 1 Zidovudine Resistance", J Clin Micro, 2777-2780;
17. Frost, S.D.W., and McLean, A.R. (1994) "Quasispecies Dynamics and the Emergence of Drug Resistance During Zidovudine Therapy of Hiv Infection", AIDS 8:323-332;
18. Holodniy, Mark, et al. (1995) "Determination of Human Immunodeficiency Virus RNA In Plasma and Cellular Viral DNA Genotypic Zidovudine Resistance Combination Therapy", J Virol, 3510-3516;
19. Kellam, P., et al. (1994) "Zidovudine Treatment Results in the Selection of Human Immunodeficiency Virus Type 1 Variants Whose Genotypes Confer Increasing Levels of Drug Resistance", J Gen Virol 75:341-351;
20. Lieven Stuyver, et al. (1997) "Line Probe Assay For Rapid Detection Of Drug Selected Mutations In The Human Immunodeficiency Virus Type 1 Reverse Transcriptase Gene", Antimicro Agen and Chemother, 284-291;
21. Mohri, H., et al. (1993) "Quantitation of Zidovudine Resistant Human Immunodeficiency Virus Type 1 in the Blood of Treated and Untreated Patients", PNAS 90:25-29;
22. Nájera, I., et al. (1994) "Natural Occurrence of Drug Resistance Mutations in the Reverse Transcriptase of Human Immunodeficiency Virus Type 1 Isolates", Aids Res Hum Retroviruses 10:1479-1488;

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23. Nájera, I., et al. (1995) "pol Gene Quasispecies of Human Immunodeficiency Virus: Mutations Associated with Drug Resistance in virus from Patients Undergoing No Drug Therapy", J Virol 69:23-31;
24. Nunberg, J.H., et al. (1990) "Viral Resistance to Human Immunodeficiency Virus Type 1-Specific Pyridinone Reverse Transcriptase Inhibitors", J Virol 65:4887-4892;
25. Richman, D.D. et al. (1994) "Nevirapine Resistance Mutations of Human Immunodeficiency Virus Type 1 Selected during Therapy", J Virol 68:1660-1666;
26. Richman, D.D. et al. (1991) "Human Immunodeficiency Virus Type 1 Mutants Resistant to Nonnucleoside Inhibitors of Reverse Transcriptase Arise in Tissue Culture", PNAS 88:11241-11245; and
27. Sanger, et al. (1977) "DNA Sequencing with Chain-terminating Inhibitors", PNAS 74:5463-5467.

Applicant also attaches as **Exhibit B** a copy of the International Search Report for PCT Application No. PCT/US99/11629, filed May 26, 1999 with the U.S. Receiving Office.

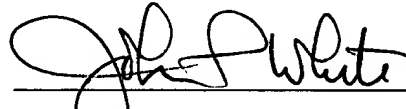
Applicant requests that the Examiner make these documents of record in the subject application.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorney invites the Examiner to telephone at the number provided below.

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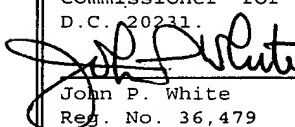
No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents Washington, D.C. 20231.



John P. White  
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12/22/99  
Date